Original articles

J. Perinat. Med.
3 (1979) 202

Normal pregnancy: A model of sustained respiratory alkalosis

Hossam E. Fadel, Gretajo Northrop, H. Robert Misenhimer, Rollie J. Harp

Dept. of Obstetrics and Gynecology and Internal Medicine, Rush Presbyterian–St. Luke's Medical Center, Chicago

Systems and Computer Services, Medical College of Georgia, Augusta, Georgia

Hyperventilation has been known to occur in pregnancy. It is believed to result from progesterone stimulation of the respiratory center [19]. Plasma bicarbonate, base excess and buffer base are all reduced in pregnancy. Most authors believe these to be compensatory changes in response to the respiratory alkalosis, [1, 19, 20] while others believe they result from an associated metabolic acidosis [15, 24].

Controversy also exists in relation to maternal oxygenation during pregnancy. Some authors reported decreased arterial oxygen tension (pO_2) and postulated that this was due to impaired oxygen transfer across the lungs [7, 26], while others reported an increased paO_2 in pregnancy [1, 3, 23, 30].

The aim of the present study was to categorize the acid-base status in normal pregnancy. Various acid base and blood gas parameters were studied in arterial blood samples obtained from normal third trimester pregnant women and the results obtained form the basis of this report. The same parameters were studied in the amniotic fluid from the same patients. These data and their correlation with the maternal blood changes are reported elsewhere [10].

1 Material and methods

Arterial blood gas analyses were performed on 59 healthy women in their third trimester of pregnancy who were to undergo amniocentesis. Their menstrual dates were accurate and did correlate with the neonatal estimation of the gestational age. Prenatal vitamins and iron supplements were the only medications taken by these patients. Informed consent was obtained. Immediately after the amniocentesis, while still supine, 20 ml of blood was collected anaerobically in a heparinized glass syringe through percutaneous radial artery puncture under local anesthesia. To a sodium fluoride containing tube 10 ml were added, 5 ml were delivered into another tube, and the heparinized syringe was immediately sealed and immersed in ice. All samples were transported immediately to the

Curriculum vitae

HOSSAM E. FADEL *was born in Egypt, 1940. He graduated from Ain Shams Medical School, Egypt, 1960. He specialized in Obstetrics and Gynecology and became an instructor, then a lecturer in Ain Shams Medical School. He moved to U.S.A. in 1970 and had fellowship in Perinatal medicine, and was appointed to the faculty of Rush Medical College, Chicago, 1973. He is presently Associate professor, Chief of Maternal-Fetal Medicine section, Medical College of Georgia, Augusta, Georgia, U.S.A.*

0300-5577/79/0007-0195$02.00

Tab. I. Results of the acid base determinations in normal third trimester pregnant women. Comparison with normal non-pregnant females.

	Oxygen tension (Torr)	Carbon dioxide tension (Torr)	Plasma bicarbonate (mEq/L)	pH	Base excess (mEq/L)	Lactate (mmol/L)	Pyruvate (mmol/L)
Normal pregnancy	99.3* ± 7.8	28.8 ± 3.7	19.0 ± 2.8	7.42 ± 0.03	−4.2 ± 2.2	1.316 ± 0.66	0.063 ± 0.04
Normal	95.0 ± 5.72	38.1 ± 2.94	23.6 ± 0.99	7.40 ± 0.03	−1.0 ± 1.44	1.0 ± 0.2	0.05 ± 0.01

*Mean ± S.D.

laboratory. Blood gas analyses were performed with a Radiometer BMS-3-MK-2. Arterial oxygen tension (paO_2), carbon dioxide tension ($paCO_2$) and pH were measured directly. Plasma bicarbonate (HCO_3^-) and base excess (BE) were derived from the SIGGARD–ANDERSEN alignment nomogram [29]. Measured amounts of blood from the fluoride tubes were transferred rapidly to tubes containing chilled trichloracetic acid and the protein free filtrate was used for lactic and pyruvic acid determinations utilizing an enzymatic method, lactic acid dehydrogenase.* All laboratory determinations were run in duplicate. Statistical analyses (t-test, correlation, regression line) were performed using a statistical package of computer programs [17, 25].

2 Results

The average age of the study patients was 23.3 ± 4.8, and their average parity was 2.2 ± 2.1. The gestational age ranged from 30 to 42 with an average of 37.5 ± 2.9 weeks. The results of the various laboratory determinations in the study patients and the corresponding values from healthy nongravid adult females are given in Tab. I. As compared to the non-pregnant state, paO_2 (99.3 ± 7.8 Torr), is slightly increased, while $paCO_2$ (28.8 ± 3.7 Torr), HCO_3^- (19.0 ± 2.8 mEq/L), and BE (−4.2 ± 2.2 mEq/L) are markedly reduced in normal third trimester pregnancy. The pH is in the high range of normal (7.42 ± 0.03). The blood lactate and pyruvate are slightly increased (1.316 ± 0.66, and 0.063 ± 0.04 mmol/L respectively). Correlations between the different measurements were calculated. Within the gestation period studied (30–42 weeks) there were no significant correlations of any of the parameters evaluated with gestational age. The pH was negatively correlated with blood pyruvate ($r = -0.367$, $P = 0.021$), but not with blood lactate, ($r = 0.228$, $P = 0.094$). There was a significant negative correlation between $paCO_2$ and blood lactate ($r = -0.497$, $P = 0.001$).

3 Discussion

Many studies of acid base balance in pregnancy have been published. However, many discrepant results and questions remain. At least some of these discrepancies are due to differences in blood sampling methods and laboratory techniques. In some studies, the blood specimens were either venous or capillary [7, 15, 24], while in others [1, 3, 6], as in this study, arterial blood specimens were utilized. The control non-pregnant values are in close agreement with those cited in previous reports [14, 29].

Maternal paO_2 was reported to be reduced in pregnancy [7, 26]. Other investigators reported higher paO_2 levels in pregnancy but stated that paO_2 did not increase as much as expected from hyperventilation [23, 30]. We found that the mean paO_2 is increased in normal pregnancy over nonpregnant values (99.3 vs 95.0 Torr), in agreement with the more recent reports [1, 3, 28]. The higher paO_2 values obtained in our study, as

*Sigma Technical Bulletin 627/826-UV, Sigma Chemical Company, St. Louis, MO. U.S.A.

well as the latter studies, compared to the previous studies, are probably due to the use of the sensitive direct polarographic technique for the measurement of the oxygen tension. The increased paO_2 in pregnancy is presumably due to the increased alveolar oxygen tension (pAO_2) [1, 23]. The latter is caused by a significant reduction in alveolar carbon dioxide tension, resulting from a significant increase of the alveolar ventilation [4], and unaltered alveolar tensions of nitrogen and water vapor. In a recent report, there was no evidence of increased arteriovenous shunting or alveolar-arterial pO_2 differences in normal pregnancy [28].

The mean $paCO_2$ in this study was 28.8 ± 3.7 Torr. Others reported the same [3] or a lower value [7], but mostly a slightly higher $paCO_2$ [1, 4, 6, 15, 24]. This is significantly lower than in adult non-pregnant females, in agreement with the previously cited studies. The reduced $paCO_2$ presumably facilitates the elimination of carbon dioxide from fetal blood across the placenta [19]. The mean pH was found to be 7.42 ± 0.03, in close agreement with others [1, 3, 6, 15, 24]. This value, which corresponds to hydrogen ion (H^+) concentration of 38 nmoles/L, is in the upper range of normal in non-pregnant females [15, 29]. Our results confirm the previously reported reduced HCO_3^- levels in normal pregnancy [1, 7, 14, 15, 24]. The mean blood BE was found to be −4.22 ± 2.22 mEq/L which is less than in normal adult women [29], in agreement with previous reports [1, 6, 7, 14, 24].

Blood lactic acid level in the normal pregnant women was 1.316 ± 0.66 mmol/L. This agrees with the average of reported values by different investigators i.e. 1.25 mmol/L, [14] and represents an increase over non-pregnant females, in agreement with the previously cited report [14]. Our value for blood pyruvic acid (0.063 ± 0.04 mmol/L) is lower than the average reported in pregnancy (0.19 mmol/L) [14] but higher than nonpregnant controls both in our study, and in the latter report [14].

In man, increase of blood lactic acid was noted to occur during either active (voluntary) or passive hyperventilation while awake or during anesthesia [27]. It has been postulated that the decrease of intracellular H^+ concentration (consequent to hyperventilation) stimulates the enzyme phospho-fructo-kinase that results in increased glycolytic production of pyruvate and consequently lactate in both tissues and red blood cells [9, 22]. The increased pyruvate and lactate levels observed in normal pregnancy may result from the same mechanism. This is supported by our finding of a statistically significant negative correlation between $paCO_2$, and blood lactate ($r = -0.497$, $P = 0.001$), and between the pH and blood pyruvate ($r = -0.367$, $P = 0.021$). Other possible sources for increased maternal lactate levels are the fetus and/or the placenta. However, the studies that were conducted during cesarean section to determine the directional transfer of lactate and pyruvate across the placenta are conflicting and non-conclusive [8, 13, 18].

Significance bands relating appropriate physiologic responses of pH (or H^+), HCO_3^- and/or BE to varying levels of $paCO_2$ under well-controlled experimental conditions have been constructed [29]. These bands show, with 95% confidence, these relationships in simple acid-base disturbances. Values lying outside these bands strongly suggest the existence of a second independent primary i.e. a mixed acid base disturbance [16, 21, 29]. Such bands have been constructed in humans for acute and chronic hypercapnia [5] and acute hypocapnia [2]. Comparable data in man with chronically adapted respiratory alkalosis are not available, the longest period of observation under controlled conditions was 26 hours [12]. However, such significance bands were generated from observations on 10 dogs exposed to hypoxemic hypocapnia for 1–2 weeks [11]. A steady state was obtained after 4–5 days of stepwise decrease in atmospheric oxygen from 21% to 9%. The mean values of H^+ and HCO_3^- as they relate to $paCO_2$ in the normal pregnant women in this study were found to be within the limits of these confidence bands. This suggests that changes of acid base balance in pregnancy are simple and not mixed i.e. sustained respiratory alkalosis without an added metabolic acidosis. When individual values were plotted, some of the pH values were below the band (Fig. 1) and some of the HCO_3^- values were above the band (Fig. 2). These particular values may represent the effect

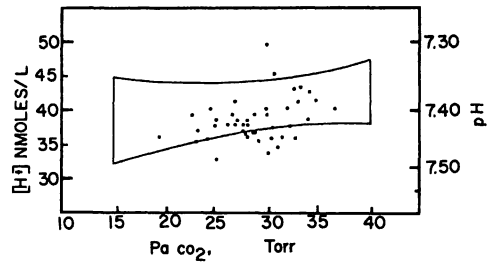


Fig. 1. Arterial carbon dioxide tension ($paCO_2$) as related to hydrogen ion concentration (H^+) in normal third trimester pregnancy. The results are superimposed on the significance band calculated by GENNARI et al. 1972 [11] for chronic hypocapnia in dogs.

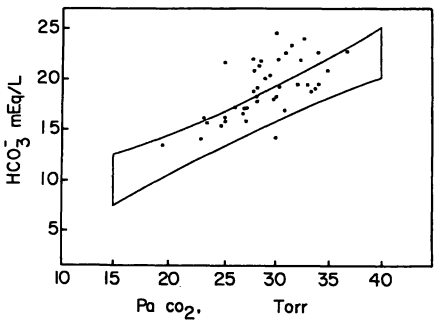


Fig. 2. Arterial carbon dioxide tension ($paCO_2$) as related to plasma bicarbonate (HCO_3^-) in normal third trimester pregnant women. The results are superimposed on the significance band calculated by GENNARI et al. 1972 (11) for chronic hypocapnia in dogs.

of temporary increased hyperventilation and further decrease in $paCO_2$ due to anxiety at the time of obtaining the blood sample. However, it is possible that these bands are not quite applicable. The experimental design used in their generation is obviously very different from the physiologic changes that occur in normal pregnant women. Therefore, we proceeded to construct from our data confidence bands correlating the H^+ concentration (pH) and HCO_3^- to $paCO_2$ levels. Regression lines were calculated from 43 cases of paired data:

$$H^+ = 28.3 + 0.335\ paCO_2$$
$$HCO_3^- = 4.63 + 0.499\ paCO_2$$

The standard error of these regression lines at the 95% level was then calculated and the bands plotted [25] (Figs. 3 and 4).

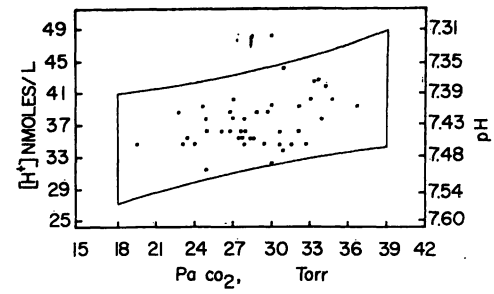


Fig. 3. Significance band showing the anticipated response of hydrogen ion activity (H^+) to changes of arterial carbon dioxide tension, ($paCO_2$) (within 95% confidence limits) in normal third trimester pregnant women.

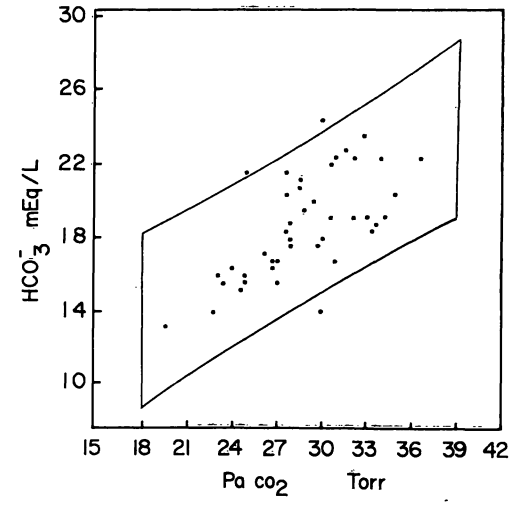
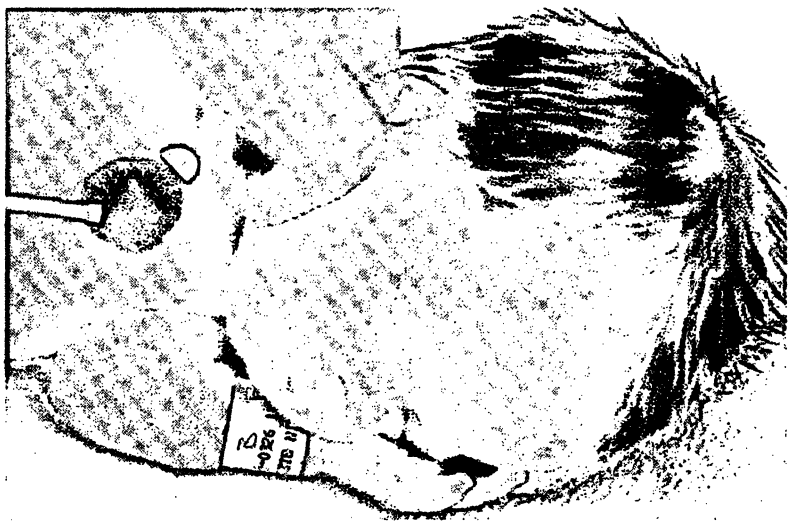


Fig. 4. Significance band showing the anticipated response of bicarbonate (HCO_3^-) to changes of arterial carbon dioxide tension, ($paCO_2$) (within 95% confidence limits) in normal third trimester pregnancy.

These bands define the 95% confidence limits for anticipated response to sustained respiratory alkalosis in normal third trimester pregnant women. Based on our data, there is no evidence of metabolic acidosis in pregnancy as has been suggested by some investigators [7, 15, 24]. The decreases in HCO_3^- and BE were well within the anticipated response for compensation of respiratory alkalosis, and there was no undue increase in blood lactic acid. Pregnancy, therefore, represents a state of "sustained respiratory alkalosis", and because the pH is still within the normal range, we do not agree with its characterization as "incompletely compensated" respiratory alkalosis [24]. The acid base status in normal pregnancy can best be characterized as "maximally compensated sustained respiratory

TCM. Radiometer's non-invasive oxygen monitor. The bloodless revolution for intensive care of babies.



The outstanding design of Radiometer's transcutaneous measuring equipment ensures the highest possible correlation to PaO_2, safeguards the patient against burning of the skin and facilitates measurements even over protracted periods.

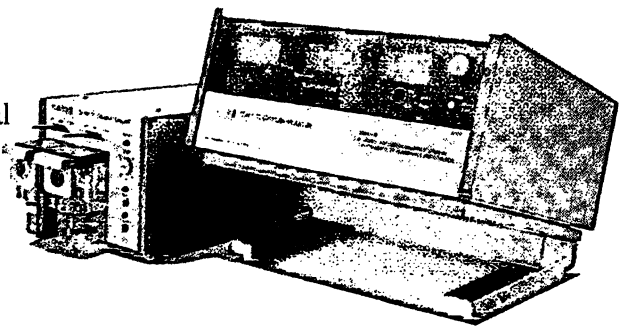
The values measured by our equipment can be correlated with other parameters on multi-channel recorders.

A special design of the electrode is available for scalp application on babies during delivery.

The Radiometer TCM1 TC Oxygen Monitor is UL-approved and conforms to IEC regulations for patient safety.

Transcutaneous Po_2

Monitoring of the oxygen status of patients in Neonatal Intensive Care has become practically possible by Radiometer's design of an innovative Po_2 electrode measuring continuously and bloodlessly through the skin of the patient. The tc-Po_2 electrode transfers heat through the skin, hyperaemizing the dermal capillaries and making the skin permeable to oxygen. Variations in oxygen status are measured by the electrode placed on the skin - continuously and without discomforting the patient.



Radiometer TCM features:

Mono-micro cathode for low comsumption
Large electrode heat-transfer area
Separate fixation ring for safety
Sterile gel for rapid heat-transfer
Audible/visual alarms for all parameters
Recorder output for all parameters
Operator-selectable temperatures, 35°-45°C
Calibration unit for high accuracy

RADIOMETER COPENHAGEN

Radiometer A/S · 72 Emdrupvej
DK-2400 Copenhagen NV · Denmark

alkalosis". Unlike acclimatization to high altitudes, which is the other example of such a status, pregnancy is not associated with hypoxemia. Pregnancy, therefore, is the best and only natural model for this type of acid base status. The significance bands relating the pH and HCO_3^- to $paCO_2$ levels constructed from these data should be useful as reference for the evaluation of the acid base status of patients with sustained respiratory alkalosis, in addition to being a useful reference for the detection of superimposed acid base distrubances in pregnant women.

Summary

The aim of this study was to categorize the acid base status in normal pregnancy. Blood gases and other acid base parameters were determined in arterial blood samples from 59 normal third trimester pregnant women.

Oxygen and carbon dioxide tensions (paO_2 and $paCO_2$), and pH were measured directly using a Radiometer BMS-3-MK-2. Plasma bicarbonate (HCO_3^-), and base excess (BE) were derived from Siggard Andersen alignment nomogram. Blood lactate and pyruvate were measured using an enzymatic; lactic dehydrogenase method. Compared to the non-pregnant state (Tab. I), paO_2 (99.3 ± 7.8 Torr), blood lactate (1.316 ± 0.66 mmol/L) and blood pyruvate (0.063 ± 0.04 mmol/L) were slightly increased, while $paCO_2$ (28.8 ± 3.7 Torr), HCO_3^- (19.0 ± 2.8 mEq/L), and BE (–4.2 ± 2.2 mEq/L) were markedly reduced. The pH (7.42 ± 0.03) was slightly increased but still in the normal non-pregnant range.

These changes are thought to be initiated by the stimulant action of progesterone on the respiratory center causing increased alveolar ventilation. The alveolar tension of CO_2 decreases while that of O_2 increases, resulting in maternal hypocapnia, and increased paO_2. The sustained hypocapnia would result in alkalosis if it were not for the compensatory mechanisms that lead to a decrease in plasma bicarbonate and base excess. The reduced H^+ concentration is known to stimulate the enzyme phosphofructokinase and cause increased glycolytic production of pyruvate and secondarily lactate. This mechanism may explain the slightly increased lactate and pyruvate levels in pregnancy.

Pregnancy, therefore, represents a state of sustained respiratory alkalosis that is compensated maximally (i.e. pH is the normal range) without evidence of superimposed metabolic acidosis. This was further supported by the fact that the mean values of H^+ and HCO_3^- as they relate to $paCO_2$ in the study patients were within the limits of the confidence bands representing chronic hypocapnia (in dogs). Because no comparable bands have been generated in man, so far, and because pregnancy represented a natural model of this unique acid base status (sustained respiratory alkalosis) without the effects of hypoxemia, as in individuals living at high altitudes or under experimental conditions, we elected to construct from the data significance bands that correlate the H^+, HCO_3^- concentrations to $paCO_2$ levels. These bands define the 95% confidence limits for anticipated response in „sustained respiratory alkalosis". These should be useful for the evaluation of the acid base status of patients with sustained respiratory alkalosis, in addition to being a useful reference for the detection of superimposed acid base disturbances in pregnant women.

Keywords: Acid base equilibrium, bicarbonate, carbon dioxide, hyperventilation, hypocapnia, lactate, oxygen, pyruvate, respiratory alkalosis, third trimester, pregnancy.

Zusammenfassung

Die normale Schwangerschaft als Modell einer beständigen respiratorischen Alkalose

Ziel dieser Arbeit war die Untersuchung des Säure-Basen-Status einer normalen Schwangerschaft. Dazu wurden in arteriellen Blutproben von 59 gesunden Schwangeren im letzten Schwangerschaftsdrittel die Blutgaswerte sowie andere Säure-Basen-Parameter bestimmt.

Der O_2- und CO_2-Partialdruck (paO_2 und $paCO_2$) wie auch der pH wurden direkt mit einem Radiometer BMS-3-MK-2 gemessen. Die Plasmabikarbonatkonzentration (HCO_3^-) und den Basenüberschuß (=base excess, BE) erhielten wir aus dem Siggaard-Andersen-Nomogramm. Der Laktat- bzw. Pyruvatspiegel im Blut wurde mit Hilfe der enzymatischen Aktivität der Laktatdehydrogenase bestimmt. Im Vergleich mit Nichtschwangeren (Tab. I) waren der paO_2 (99.3 ± 7.8 Torr), der Laktatspiegel (1.316 ± 0.66 mmol/l) und der Pyruvatspiegel (0.063 ± 0.04 mmol/l) leicht erhöht. Deutlich erniedrigt dagegen waren der $paCO_2$ (28.8 ± 3.7 Torr), die HCO_3-Konzentration (19.0 ± 2.8 mäq/l) und der BE (–4.2 ± 2.2 mäq/l). Der pH war mit 7.42 ± 0.03 leicht erhöht, jedoch noch innerhalb der normalen Schwankungsbreite.

Diese Änderungen werden als ein stimulierender Effekt des Progesterons auf das Atemzentrum gedeutet, wodurch eine gesteigerte alveoläre Ventilation ausgelöst wird. Die Folgen sind ein verminderter alveolärer pCO_2 gegenüber einem erhöhten pO_2 in der Alveolarluft. Das bedeutet, daß sich im mütterlichen arteriellen Blut eine Hypokapnie und ein erhöhter paO_2 einstellt. Diese andauernde Hypokapnie würde eine Alkalose zur Folge haben, die jedoch durch die kompensatorische Maß-

nahme der HCO_3--Erniedrigung und damit der Herabsetzung des BE verhindert wird. Weiter ist bekannt, daß eine verminderte H^+-Ionenkonzentration einen Stimulus für die Aktivität der Phosphofruktokinase darstellt und auf diesem Weg die Glykolyse gesteigert wird, d.h. mehr Pyruvat und letztlich auch Laktat produziert wird. Über diesen Mechanismus könnten die leicht erhöhten Laktat- und Pyruvatspiegel in der Schwangerschaft erklärt werden.

Die Schwangerschaft stellt damit einen Zustand der beständigen respiratorischen Alkalose dar, die jedoch voll kompensiert ist (pH = normal), ohne daß Anzeichen für eine überlagernde metabolische Azidose erkennbar sind. Diese Interpretation ließ sich durch folgende Beobachtung weiter stützen: wir fanden, daß die mittleren H^+- und HCO_3-Konzentrationen als Funktion des $paCO_2$ bei den untersuchten Patienten innerhalb von Vertrauensbereichen lagen, die man für chronische Hypokapnien (bei Hunden) aufgestellt hat. Für den Menschen wurden vergleichbare Kurven nicht entwickelt. Da die Schwangerschaft aber ein natürliches Modell dieses abweichenden Säure-Basen-Status darstellt, ohne daß sich Anzeichen einer Hypoxämie wie bei Menschen in großen Höhen oder unter experimentellen Bedingungen einstellen, nutzten wir die gewonnenen Daten zur Erstellung von Signifikanzbereichen, die die H^+ bzw. HCO_3-Konzentrationen mit dem $paCO_2$ korrelieren. Mit diesen Bereichen definierten wir die 95%- Vertrauensschranken für bestimmte Erwartungswerte bei „beständiger respiratorischer Alkalose." Ein praktischer Nutzen liegt in der Untersuchung des Säure-Basen-Haushalts von Patienten mit chronischer respiratorischer Alkalose. Darüberhinaus könnte dadurch eine Hilfestellung bei der Aufdeckung von überlagernden Säure-Basen-Störungen in der Schwangerschaft gegeben werden.

Schlüsselwörter: Bikarbonat, Kohlendioxyd, Hyperventilation, Hypokapnie, Laktat, Pyruvat, respiratorische Alkalose, Säure-Basen-Haushalt, Sauerstoff.

Résumé

Grossesse normale: Un modèle d'alcalose respiratoire soutenue

Cette étude a eu pour but de catégoriser le statut acido-basique de la grossesse normale. Les gaz sanguins et autres paramètres acido-basiques ont été définis dans des spécimens de sang artériel de 59 parturientes au troisième trimestre d'une grossesse normale.

Nous avons mesuré directement à l'aide d'un radiomètre BMS-3-MK-2 les tensions d'oxygène et de dioxide de carbone (paO_2 et $paCO_2$) ainsi que le pH. Le bicarbonate du plasma (HCO_3) et l'excès basique (BE) ont été dérivés du nomogramme d'alignement de siggard Andersen. Le sel lactique et le pyruvate sanguins ont été mesurés à l'aide d'un enzymatique (méthode de dehydrogénase lactique). Comparés à l'état de non-grossesse (**Tab. I**), le paO_2 (99,3 ± 7,8 Torr), le sel lactique du sang (1,316 ± 0,66 mmol/L) et le pyruvate du sang (0,063 ± 0,04 mmol/L) ont légèrement augmenté, tandis que le $paCO_2$ (28,8 ± 3,7 Torror), le HCO_3- (19,0 ± 2,8 mEq/L), et le BE (–4,2 ± 2,2 mEq/L) ont nettement baissé. Le pH (7,42 ± 0,03) a légèrement augmenté tout en restant dans les normes de la non-grossesse.

Ces changements sont dûs sans doute à l'action stimulante du progestérone sur le centre respiratoire causant une ventilation alvéolaire accrue. La tension alvéolaire deCO_2 diminue tandis que celle de O_2 augmente, causant une hypoxapnie maternelle et un Pao_2 accru. L'hypocapnie soutenue causerait une alcalose sans les mécanismes compensateurs provoquant une réduction du bicarbonate du plasma et de l'excès basique. La concentration réduite de H^+, comme on sait, stimule la phosphofructocinase enzymatique et cause une production glycolytique accrue de pyruvate et de sel lactique secondaire. Ce mécanisme peut expliquer la hausse légère de sel lactique et de pyruvate dans la grossesse. En conséquence, la grossesse représente un état d'alcalose respiratoire soutenue qui est compensée au maximum (c.à.d. que le pH reste normal) sans évidence d'acidose métabolique superposée. Cette hypothèse a été renforcée par le fait que les valeurs moyennes de H^+ et de HCO_3- dans leurs rapports avec $paCO_2$ chez les parturientes examinées sont restées dans les limites des bandes précises représentant l'hypocapnie chronique (chez les chiens). Etant donné qu.aucune bande comparable n'a été produite jusque là chez l'homme et que la grossesse a constitué un modèle naturel de ce statut acidobasique unique (alcalose respiratoire soutenue) sans les effets d'hypoxémie, comme chez les individus vivant à haute altitude ou dans des conditions expérimentales, nous avons choisi de nous baser sur les données des bandes significatives qui établissent des corrélations entre les concentrations de H^+ et de HCO_3^- et les degrés de $paCO_2$. Ces bandes définissent les limites à 95% de précision pour la réaction anticipée d'une «alcalose respiratoire soutenue». Celles-ci devraient être utiles pour l'évaluation du statut acido-basique des sujets avec alcalose respiratoire soutenue et servir de référence pour le dépistage des troubles acido-basiques superposés chez les femmes enceintes.

Mots-clés: Alcalose respiratoire, bicarbonate, dioxide de carbone, équilibre acido-basique, hyperventilation, hypocapnie, oxygène, pyruvate, sel lactique, troisième trimestre de grossesse.

Acknowledgement: This work was supported in part by a Grant Number 37133, Research Committee of Rush Presbyterian-St. Luke's Medical Center.

The authors express their appreciation to Dr. WILLIAM A. SPEIR, Jr., Pulmonary Medicine Section, Department of Medicine, Medical College of Georgia, for his review of the manuscript and his helpful suggestions.

Bibliography

[1] ANDERSEN, G. J., G. B. JAMES, N. P. MATHERS, E. L. SMITH, J. WALKER: The maternal oxygen tension and acid base status during pregnancy. J. Obstet. Gynaec. Brit. Cwlth. 76 (1969) 16

[2] ARBUS, G. S., L. A. HEBERT, P. R. LEVESQUE, B. E. ETSTEN, W. B. SCHWARTZ: Characterization and clinical application of the „Significance Band" for acute respiratory alkalosis. N. Engl. J. Med. 280 (1969) 117

[3] BLECHNER, J. N., J. R. COTTER, V. G. STENGER, C. M. HINKLEY, H. PRYSTOWSKY: Oxygen, carbon dioxide, and hydrogen ion concentrations in arterial blood during pregnancy. Amer. J. Obstet. Gynecol. 100 (1968) 1

[4] BONICA, J. J.: Basic considerations. Clin. Obstet. Gynaec. 2 (1975) 469

[5] BRACKETT, N. C., Jr.: An approach to clinical disorders of acid base balance. South. Med. J. 67 (1974) 1084

[6] COHEN, A. V., H. SCHULMAN, S. L. ROMNEY, F. MAIER: Maternal acid base metabolism in normal human parturition. Amer. J. Obstet. Gynecol. 107 (1970) 933

[7] DAYAL, P., Y. MURATA, H. TAKAMURA: Antepartum and postpartum acid base changes in maternal blood in normal and complicated pregnancies. J. Obstet. Gynaec. Brit. Cwlth. 79 (1972) 612

[8] DEROM, R.: Anaerobic metabolism in the human fetus. In: The normal delivery. Amer. J. Obstet. Gynecol. 89 (1964) 241

[9] ELDRIDGE, F., J. SALZER: Effect of respiratory alkalosis on blood lactate and pyruvate in humans. J. Appl. Physiol. 22 (1967) 461

[10] FADEL, H. E., G. NORTHROP, H. R. MISENHIMER, R. J. HARP: Acid base determinations in amniotic fluid and blood of normal late pregnancy. Obstet. Gynecol. 53 (1979) 99

[11] GENNARI, F. J., M. B. GOLDSTEIN, W. B. SCHWARTZ: The nature of the renal adaptation to chronic hypocapnia. J. Clin. Invest. 51 (1972) 1722

[12] GLEDHILL, N., G. J. BEIRNE, J. A. DEMPSEY: Renal response to short term hypocapnia in Man. Kidney Int. 8 (1975) 376

[13] HENDRICKS, C. H.: Studies on lactic acid metabolism in pregnancy and labor. Amer. J. Obstet. Gynecol. 73 (1957) 492

[14] KIRSCHBAUM, T. H., J. C. DEHAVEN: Maternal-fetal blood constituents. In: ASSALI, N. S.: Biology of gestation, vol II. The fetus and neonate. Academy Press, Inc., New York, 1968

[15] MACRAE, D. J., D. PALAVRADJI: Maternal acid base changes in pregnancy. J. Obstet. Gynaec. Brit. Cwlth. 74 (1967) 11

[16] MCCURDY, D. K.: Mixed metabolic and respiratory acid base disturbances. Diagnosis and treatment. Chest. 62 (Suppl 2) (1972) 35 s

[17] NIE, N. H., C. H. HALL, J. G. JENKINS, K. STEINBRENNER, D. H. BENT: Statistical package for the social sciences. Second edition. McGraw Hill Book Company, New York, 1975

[18] OTEY, E., V. STENGER, D. EITZMAN, T. ANDERSEN, I. GESSNER, H. PRYSTOWSKY: Movements of lactate and pyruvate in the pregnant uterus of the human. Amer. J. Obstet. Gynecol. 90 (1964) 747

[19] PROWSE, C. M., E. A. GAENSLER: Respiratory and acid base changes during pregnancy. Anesthesiology 26 (1965) 381

[20] PRYSTOWSKY, H., A. E. HELLEGERS, P. D. BURNS: Comparative study of alkaline reserve of normal and pregnant women. Amer. J. Obstet. Gynecol. 82 (1961) 1295

[21] RASTEGAR, A., S. O. THIER: Physiologic consequences and bodily adaptations to Hyper- and Hypocapnia. Chest 62, (Suppl 2) (1972) 28

[22] RELMAN, A. S.: Metabolic consequences of acid base disorders. Kidney Int. 1 (1972) 347

[23] ROSSIER, P. H., A. BUHLMANN, K. WIESINGER: Physiologie und pathophysiologie der Atmung. Springer-Verlag, Berlin, 1956

[24] SJOSTEDT, S.: Acid base balance of arterial blood during pregnancy and in the puerperium. Amer. J. Obstet. Gynecol. 84 (1962) 775

[25] SOKAL, R. R., F. J. ROHLF: Biometry. W. H. Freeman and Company, San Francisco, 1969

[26] STENGER, V., D. EITZMAN, T. ANDERSEN, C. D. PADUA, I. GESSNER, H. PRYSTOWSKY: Observations on the placental exchange of the respiratory gases in pregnant women at cesarean section. Amer. J. Obstet. Gynecol. 88 (1964) 45

[27] SYKES, M. K., P. M. COOKE: The effect of hyperventilation on "excess lactate" production during anesthesia. Brit. J. Anaesth. 37 (1965) 372

[28] TEMPLETON, A., G. R. KELMAN: Maternal blood gases, (PAo_2–Pao_2), physiological shunt and VD/VT in normal pregnancy. Brit. J. Anaesth. 48 (1976) 372

[29] WINTERS, R. W., K. ENGEL, R. B. DELL, R. P. BERKSON: Acid base physiology in medicine. A self instruction program. Second edition. The London Company of Cleveland and Radiometer A/S of Copenhagen, Cleveland, 1967

[30] WULF, H.: A comparative study of actual blood bases and acid base metabolism in maternal and fetal blood during parturition. In: HORSKY, J., Z. K. STEMBERA: Intrauterine dangers to the fetus, Excerpta Medica, Amsterdam, 1967

Received August 25, 1978. Accepted February 2, 1979.

Dr. Hossam E. Fadel
Department of Obstetrics and Gynecology
Medical College of Georgia
Augusta, Georgia 30902/USA